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SYNTHESIS OF SACCHARINIC ACID DERIVATIVES*

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ABSTRACT

Hydroxylation of ethyl *cis*-2,3-dideoxy-4,5-*O*-isopropylidene-2-*C*-methyl-DL-*glycero*-pent-2-enonate (**1**) with osmium tetraoxide gave ethyl 4,5-*O*-isopropylidene-β-DL-galactosaccharinate (ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-DL-lyxonate, **3**) and ethyl 4,5-*O*-isopropylidene-α-DL-glucosaccharinate (ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-DL-ribonate, **4**). Similarly, the *trans*-isomer of **1** yielded a mixture of ethyl 4,5-*O*-isopropylidene-α-DL-galactosaccharinate (ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-DL-xylonate, **5**) and ethyl 4,5-*O*-isopropylidene-β-DL-glucosaccharinate (ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-DL-arabinonate, **6**). Compounds **3–6** were transformed into the corresponding 1,4-lactones.

INTRODUCTION

We have described[2] the use of the Knoevenagel–Doebner reaction in the synthesis of hexuloses, deoxyhexuloses, and branched-chain deoxyhexuloses, and now report an extension of this method to the synthesis of some derivatives of saccharinic acids.

Saccharinic acids are formed on treatment[3] of sugars with alkali. Of the possible[3] C-5 saccharinic acids, α-D-[4] and α-L-gluco-[5], β-D-[6] and β-L-gluco-[4b,e], α-D-[6] and α-L-galacto-[7], and β-D-[6] and β-L-galacto-saccharinic acid[7] are known. We now report a new synthesis of some of the above compounds.

RESULTS AND DISCUSSION

Hydroxylation of ethyl *cis*-2,3-dideoxy-4,5-*O*-isopropylidene-2-*C*-methyl-DL-*glycero*-pent-2-enonate (**1**)[2c,8] with osmium tetraoxide gave a mixture of ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-DL-lyxonate (**3**) and ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-DL-ribonate (**4**) and, in the same way, the *trans*-isomer (**2**) of **1** gave a mixture of ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-DL-xylonate (**5**) and ethyl 4,5-*O*-iso-

*Branched-chain Sugars, Part VII. For Part VI, see ref. 1.
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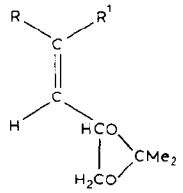
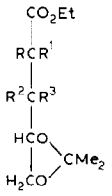
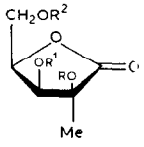
propylidene-2-*C*-methyl-DL-arabinonate (**6**). Compound **3–6** were isolated as the DL forms by chromatography.



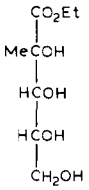
1 R = Me, R^1 = CO_2Et
2 R = CO_2Et, R^1 = Me



3 R = R^2 = OH, R^1 = Me, R^3 = H
4 R = Me, R^1 = R^3 = OH, R^2 = H
5 R = Me, R^1 = R^2 = OH, R^3 = H
6 R = R^3 = OH, R^1 = Me, R^2 = H



7 R = R^1 = R^2 = H
8 R, R^1 = CMe_2, R^2 = H
9 R, R^1 = CMe_2, R^2 = Ac
10 R = R^1 = R^2 = Bz



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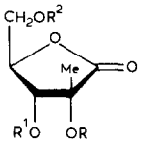
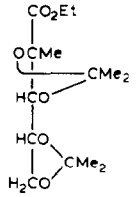


12 R = R^1 = R^2 = H
13 R, R^1 = CMe_2, R^2 = H
14 R, R^1 = CMe_2, R^2 = Ac
15 R = R^1 = R^2 = Bz

DL Compounds are depicted as D enantiomers

The configurations of **3** and **4** were established by transformation into the corresponding 2-*C*-methylpentono-1,4-lactones **7** and **12**. Although the ^{1}H-n.m.r. spectra of **7** and **12** showed H-3 as a doublet with $J_{3,4}$ 3.75 and 7.5 Hz, respectively, in close agreement with the values of 4 and 7.1 Hz previously reported[6] for *lyxo* and *ribo* configurations, their optical rotations indicated[8] that they were near-racemic mixtures. In order to confirm the configurations assigned to **7** and **12**, the 2,3-*O*-isopropylidene derivatives (**8** and **13**) and the 2,3,5-tribenzoates (**10** and **15**) were prepared. The spectroscopic data for these derivatives were in agreement with those reported[4d,7]. Spectroscopic data for the 5-acetates (**9** and **14**) of **8** and **13** also confirmed the structures proposed for **7** and **12**, as well as those of their parent compounds **3** and **4**.

In a similar way, the *arabino* configuration of **6** was established by hydrolysis followed by reacetonation to yield three compounds identified as ethyl 2,3:4,5-di-*O*-isopropylidene-2-*C*-methyl-DL-arabinonate (**16**), 3,4-*O*-isopropylidene-2-*C*-methyl-DL-arabinono-1,5-lactone (**17**), and 2-*C*-methyl-DL-arabinono-1,4-lactone (**18**). Thus, **16** showed i.r. absorption for ester carbonyl at 1750 cm^{-1} but none for hydroxyl, and the ^{1}H-n.m.r. and mass-spectral data (see Experimental) con-



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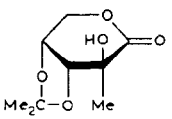
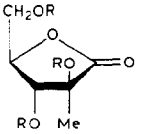
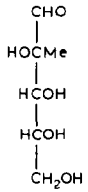


17



18 R = H
19 R = Bz
20 R = Ac



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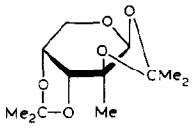

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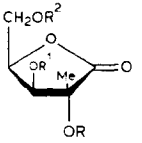

23 R = R^1 = R^2 = H
24 R = H, R^1, R^2 = CMe_2
25 R = Ac, R^1, R^2 = CMe_2

DL Compounds are depicted as D enantiomers

firmed the proposed structure. Compound **17** showed i.r. absorption at 3460 cm^{-1} associated with the tertiary HO-2, which corresponded to the ^{1}H-n.m.r. singlet at δ 3.18 that disappeared on addition of D_2O. The i.r. absorption at 1735 cm^{-1} was characteristic of a δ-lactone. The structure of **18** was determined on the basis of its analytical and spectroscopic data, by transformation into the tribenzoate (**19**) and triacetate (**20**), and by reduction to 2-*C*-methyl-DL-arabinose (**21**) followed by acetonation to give the di-*O*-isopropylidene derivative (**22**), the spectroscopic data for which were the same as those for the D form (prepared[4c] as for the L form). The formation of **16** could proceed *via* **6** or its deisopropylidenated product, whereas the formation of **17** must imply total hydrolysis of **6** to give **18** and subsequent reaction with acetone. On the basis of the foregoing results, the DL-*xylo* configuration was assigned to **5**.

Hydroxylation of D-**2**[8] yielded D-**5** and D-**6** with $[\alpha]_D$ values of $-15°$ and $+21°$, respectively. The structure of D-**6** was determined by some of the transformations applied to DL-**6**. Similarly, the transformation of D-**5** into the related 1,4-lactone (D-**23**; the physical and spectroscopic data of which accorded with those reported[6,7]), followed by acetonation to give the 3,5-*O*-isopropylidene derivative (D-**24**), demonstrated the D-*xylo* configuration. The analytical and spectroscopic data for the 2-acetate (D-**25**) of D-**24** also confirmed the proposed structure.

EXPERIMENTAL

General methods. — Melting points were determined with a Reichter hot-plate microscope and are uncorrected. Solutions were dried over $MgSO_4$ and concentrated under diminished pressure. ^{1}H-N.m.r. spectra were recorded with a Perkin–Elmer R20B or Bruker WP-80 spectrometer for solutions in $CDCl_3$ (internal Me_4Si) unless otherwise stated. I.r. spectra were recorded with a Pye Unicam SP 1000 spectrophotometer and mass spectra with a Hewlett–Packard 5930A Mass Spectrometer. Optical rotations were measured for solutions in chloroform (1-dm tube) with a Perkin–Elmer 141 Polarimeter. T.l.c. was performed on Silica Gel G (Merck), with detection by charring with sulfuric acid. Column chromatography was performed on Silica Gel (Merck, 7734). Descending p.c. was performed on Whatman No. 1 paper with 1-butanol–ethanol–water (28:7:13), and detection with silver nitrate[9].

Hydroxylation of ethyl cis-*2,3-dideoxy-4,5-*O-*isopropylidene-2-*C-*methyl-*DL-glycero-*pent-2-enonate* (**1**). — To a solution of **1**[2c] (2.6 g, 12 mmol) in ethanol–water (1:1, 25 mL) was added a solution of potassium chlorate (0.76 g, 6.2 mmol) in the same solvent (25 mL). The mixture was acidified (pH ~3.5) with acetic acid (0.5 mL), and then aqueous 1% osmium tetraoxide (5 mL) was added. The mixture was left at room temperature for 24 h. T.l.c. (ether–hexane, 2:1) then revealed that **1** had disappeared, and that two new products (R_F 0.27 and 0.18) were present. The mixture was neutralised (anhydrous K_2CO_3) and concentrated. The residue was extracted with ethyl acetate, the extract was concentrated, and the residue was subjected to column chromatography (ether–hexane, 1:2→1:1). Eluted first was syrupy ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-DL-lyxonate (**3**; 1.1 g, 37%), $[\alpha]_D$ −0.4° (*c* 1.1); ν_{max}^{film} 3460 (OH), 1740 (ester C=O), 1380 and 1370 (CMe_2), 1055 and 855 cm^{-1} (dioxolane ring). N.m.r. data: δ 4.59–3.83 (m, 4 H, H-3,4,5,5′), 4.34 (q, 2 H, J_{CH_2Me} 7 Hz, OCH_2Me), 3.73 and 2.85 (2 bs, 2 H, HO-2,3), 1.45, 1.42, and 1.38 (3 s, 9 H, Me-2 and CMe_2), and 1.35 (t, 3 H, OCH_2Me).

Anal. Calc. for $C_{11}H_{20}O_6$: C, 53.21; H, 8.12. Found: C, 53.21; H, 7.46.

Eluted second was ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-DL-ribonate (**4**; 1 g, 33%), m.p. 75–77° (from hexane–ether), $[\alpha]_D$ −0.8° (*c* 1); ν_{max}^{KBr} 3380 (OH), 1750 (ester C=O), 1385 and 1375 (CMe_2), 1050 and 845 cm^{-1}(dioxolane ring). N.m.r. data: 4.62–3.63 (m, 6 H, OCH_2Me, H-3,4,5,5′), 3.78 and 2.88 (2 bs, 2 H, HO-2,3), 1.51, 1.38, and 1.32 (3 s, 9 H, Me-2 and CMe_2), and 1.32 (t, 3 H, OCH_2Me).

Anal. Found: C, 53.05; H, 8.16.

Hydroxylation of ethyl trans-*2,3-dideoxy-4,5-*O-*isopropylidene-2-*C-*methyl-*DL-glycero-*pent-2-enonate* (**2**). — A solution of **2**[2c] (2 g, 9.3 mmol) in ethanol–water (1:1, 25 mL) was allowed to react with potassium chlorate (700 mg, 5.7 mmol), acetic acid (0.3 mL), and aqueous 1% osmium tetraoxide (3 mL). Following the above procedure, the product isolated contained two components (R_F 0.28 and 0.25; ether–hexane, 2:1). Column chromatography (ether–hexane, 1:2→1:1) of this mixture gave, first, ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-DL-xylonate (**5**;

507 mg, 22%), m.p. 65–67° (from light petroleum), $[\alpha]_D$ +0.6° (*c* 1.57); ν_{max}^{KBr} 3430 (OH), 1730 (ester C=O), 1375 and 1370 (CMe_2), 1055 and 850 cm^{-1} (dioxolane ring). ^{1}H-N.m.r. data (80 MHz): δ 4.42 (o, 1 H, $J_{3,4}$ 2.54, $J_{4,5}$ 6.30, $J_{4,5'}$ 7.75 Hz, H-4), 4.26 (q, 2 H, J_{CH_2Me} 7 Hz, OCH_2Me), 4.08 (dd, 1 H, $J_{5,5'}$ 7.75 Hz, H-5), 3.88 (t, 1 H, H-5′), 3.58 (dd, 1 H, H-3), 3.56 (bs, 1 H, HO-2), 2.86 (d, 1 H, $J_{HO,3}$ 9.65 Hz, HO-3), 1.46, 1.41, and 1.36 (3 s, 9 H, Me-2 and CMe_2), and 1.32 (t, 3 H, OCH_2Me).

Anal. Calc. for $C_{11}H_{20}O_6$: C, 53.21; H, 8.12. Found: C, 53.63; H, 8.35.

Eluted second was ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-DL-arabinonate (**6**; 1.15 g, 50%), m.p. 67–68° (from light petroleum), $[\alpha]_D$ +0.7° (*c* 1.5); ν_{max}^{KBr} 3400 (OH), 1730 (ester C=O), 1375 and 1370 (CMe_2), 1060 and 860 cm^{-1} (dioxolane ring). ^{1}H-N.m.r. data (80 MHz): δ 4.28 (q, 2 H, J_{CH_2Me} 7 Hz, OCH_2Me), 4.36–3.96 (m, 3 H, H-4,5,5′), 3.90 (dd, 1 H, $J_{3,4}$ 4.80, $J_{HO,3}$ 7.20 Hz, H-3), 3.62 (s, 1 H, HO-2), 2.55 (d, 1 H, HO-3), 1.44, 1.41, and 1.35 (3 s, 9 H, Me-2 and CMe_2), and 1.31 (t, 3 H, OCH_2Me).

Anal. Found: C, 53.49; H, 8.36.

*2-C-Methyl-*DL*-lyxono-1,4-lactone* (**7**). — A solution of **3** (0.9 g, 3.6 mmol) in acetic acid–water 1:1 (25 mL) was heated at 40° for 1 h. T.l.c. then showed that **3** had disappeared, and evaporation of the solvent gave a syrupy residue (845 mg). A solution of this residue (145 mg) in M sodium hydroxide (2 mL) was kept at 40–50° for 1 h, and then neutralised with Amberlite IR-120 (H^+) resin (5 mL). The resin was collected and washed with water, and the combined filtrate and washings were concentrated. Column chromatography (ether–methanol, 10:1) of the residue gave syrupy **7** (115 mg), $[\alpha]_D$ +4° (*c* 1.75, water), {*cf.* −79° for the L enantiomer[7]}, R_F 0.34 (ether–methanol, 10:1), R_F 0.60 (p.c.); ν_{max}^{film} 3400 (OH) and 1770 cm^{-1} (γ-lactone C=O). N.m.r. data (acetone-d_6): δ 5.01–3.50 (m, 7 H, H-3,4,5,5′, HO-3,4,5) and 1.40 (s, 3 H, Me-2); (acetone-d_6 + D_2O): δ 4.58 (o, 1 H, $J_{3,4}$ 3.75, $J_{4,5}$ 5.25, $J_{4,5'}$ 6.75 Hz, H-4), 4.15 (d, 1 H, H-3), 3.81 (m, 2 H, H-5,5′), and 1.40 (s, 3 H, Me-2).

Conventional treatment of **7** (100 mg, 0.6 mmol) with pyridine (2 mL) and benzoyl chloride (0.5 mL) at 0° gave the tribenzoate **10** (280 mg, 86%), m.p. 110–111°, $[\alpha]_D$ +1° (*c* 1.1) {lit.[7] L form, m.p. 109–110.5°, $[\alpha]_D^{17}$ −76° (*c* 2.1)}, R_F 0.66 (benzene–ethyl acetate, 1:1); ν_{max}^{KBr} 1830 (γ-lactone C=O), 1735 (benzoate C=O), and 700 cm^{-1} (benzoate). N.m.r. data: δ 8.10–6.90 (2 m, 15 H, 3 Bz), 6.05 (d, 1 H, $J_{3,4}$ 6 Hz, H-3), 5.13 (dt, 1 H, $J_{4,5}$ 5.25 Hz, H-4), 4.68 (d, 2 H, 2 H-5), and 1.92 (s, 3 H, Me-2). Mass spectrum: *m/z* 352 (M^+ − BzOH), 231 (M^+ − BzOH − BzO), 105 (Bz^+, base peak), and 77 $(Ph)^+$.

Anal. Calc. for $C_{27}H_{22}O_8$: C, 68.35; H, 4.67. Found: C, 68.21; H, 4.41.

*2,3-O-Isopropylidene-2-C-methyl-*DL*-lyxono-1,4-lactone* (**8**). — A solution of **7** (160 mg, 1 mmol) in dry acetone (10 mL) and conc. sulfuric acid (0.05 mL) was stirred with anhydrous copper sulfate (1 g) for 7 h. T.l.c. (benzene–ethyl acetate, 1:1) then revealed the presence of a product of R_F 0.38. The mixture was filtered and neutralised with Lewatid MP-69 (HCO_3^-) resin. The resin was collected, and

washed with acetone, and the combined filtrate and washings were concentrated to dryness. Column chromatography (benzene–ethyl acetate, 1:1) of the residue gave **8** (115 mg), m.p. 83–84°, $[\alpha]_D$ +3° (*c* 1.8) (*cf.* −75° for the L isomer[7]); ν_{max}^{film} 3480 (OH), 1795 (γ-lactone C=O), and 1375 cm^{-1} (CMe_2). N.m.r. data: δ (acetone-d_6) 4.71–4.41 (m, 1 H, H-4), 4.60 (s, 1 H, H-3), 4.23–3.68 (m, 3 H, H-5,5′ and HO-5), 1.53 (s, 3 H, Me-2), and 1.34 (s, 6 H, CMe_2).

Anal. Calc. for $C_9H_{14}O_5$: C, 53.47; H, 6.93. Found: C, 53.42; H, 6.83.

Conventional treatment of **8** (100 mg, 0.5 mmol) with pyridine (2 mL) and acetic anhydride (1 mL) gave the 5-acetate **9** (110 mg, 91%), m.p. 67–68°, $[\alpha]_D$ +2° (*c* 1.74), R_F 0.42 (ethyl acetate–light petroleum, 1:1); ν_{max}^{film} 1790 (γ-lactone C=O), 1745 (acetate C=O), 1375 (CMe_2), and 1240 cm^{-1} (acetate C-O). N.m.r. data: δ 4.83–4.20 (m, 4 H, H-3,4,5,5′), 2.10 (s, 3 H, Ac), 1.54 (s, 3 H, Me-2), and 1.39 (s, 6 H, CMe_2). Mass spectrum: *m/z* 245 (M^+ + 1), 229 (M^+ − Me), 216 (M^+ − CO), 186 (M^+ − Me_2CO), 184 (M^+ − AcOH), 169 (M^+ − Me − AcOH), 159, 143, 142, 141, 140, 126 (M^+ − Me_2CO − AcOH), 117, 115, 114, 113, 100, 99, 85, 83, 71, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 54.41; H, 6.75.

*Ethyl 2-C-methyl-*DL*-ribonate* (**11**). — A suspension of **4** (248 mg, 1 mmol) in acetic acid–water (1:4, 5 mL) was heated at 40° for 1 h. Dissolution occurred, and t.l.c. (ether–hexane, 2:1) then revealed that no **4** remained. Evaporation of the solvent gave **11** (185 mg, 89%), m.p. 125–127° (from ethanol–ether), $[\alpha]_D$ 0° (*c* 1.1, ethanol); ν_{max}^{KBr} 3400 and 3320 (OH), and 1750 cm^{-1} (ester C=O). N.m.r. data: δ (D_2O) 4.50–3.55 (m, 6 H, OCH_2Me, H-3,4,5,5′), 1.45 (s, 3 H, Me-2), and 1.25 (t, 3 H, *J* 7.5 Hz, OCH_2Me).

Anal. Calc. for $C_8H_{16}O_6$: C, 46.15; H, 7.69. Found: C, 45.91; H, 7.53.

*2-C-Methyl-*DL*-ribono-1,4-lactone* (**12**). — A solution of **11** (458 mg, 2.27 mmol) in water (2 mL) that contained sodium hydroxide (0.13 g, 3.25 mmol) was kept at 40° for 1 h, and then treated as for **7**. Evaporation of the solvent gave **12** (356 mg), m.p. 150–154°. Purification by column chromatography (ether–methanol, 10:1) gave material having m.p. 155–156°, $[\alpha]_D$ +3° (*c* 1, water) {lit[4a] m.p. 162–163°, $[\alpha]_D$ +93.6° (*c* 3.2, water), for the D isomer}, R_F 0.68 (p.c.); ν_{max}^{KBr} 3410 and 3330 (OH), and 1750 cm^{-1} (γ-lactone C=O). N.m.r. data (D_2O): δ 4.48 (o, 1 H, H-4), 4.06 (dd, 1 H, $J_{4,5}$ 3, $J_{5,5'}$ 15.5 Hz, H-5), 4.05 (d, 1 H, $J_{3,4}$ 7.5 Hz, H-3), 3.75 (dd, 1 H, $J_{4,5'}$ 4.5 Hz, H-5′), and 1.42 (s, 3 H, Me-2). Mass spectrum: *m/z* 163 (M^+ + 1), 162 (M^+), 145 (M^+ − OH), 144 (M^+ − H_2O), 135, 127, 117 (M^+ − OH − CO), 116 (M^+ − H_2O − CO), 103, 101, 99, 87, 74, and 43 (Ac^+, base peak).

Anal. Calc. for $C_6H_{10}O_5$: C, 44.44; H, 6.22. Found: C, 44.82; H, 6.13.

Conventional treatment of **12** (60 mg, 0.37 mmol) with dry pyridine (1 mL) and benzoyl chloride (0.2 mL) gave the tribenzoate **15** (140 mg, 80%), m.p. 134–135° (from carbon tetrachloride), $[\alpha]_D$ −0.5° (*c* 1.4) {lit.[4b] m.p. 141.5–142°, $[\alpha]_D$ +124.6° (*c* 1) for the L form}, R_F 0.66 (benzene–ethyl acetate, 1:1); ν_{max}^{KBr} 1790 (γ-lactone C=O), 1750 and 1729 (benzoate C=O), and 695 cm^{-1} (benzoate). N.m.r.

data: δ (CCl_4) 8.15–6.90 (2 m, 15 H, 3 Bz), 5.48 (d, 1 H, $J_{3,4}$ 6 Hz, H-3), 5.05 (m, 1 H, H-4), 4.68 (m, 2 H, H-5,5'), and 1.89 (s, 3 H, Me-2). Mass spectrum: *m/z* 474 (M^+), 352 (M^+ – BzOH), 231 (M^+ – BzOH – BzO), 227, 189, 176, 122 ($BzOH^+$), 105 (Bz^+, base peak), and 77 (Ph^+).

*2,3-O-Isopropylidene-2-C-methyl-*DL*-ribono-1,4-lactone* (**13**). — A suspension of **12** (120 mg, 0.7 mmol) in dry acetone (10 mL) and conc. sulfuric acid (0.05 mL) was stirred with anhydrous copper sulfate (1 g) for 7 h. T.l.c. (ethyl acetate–hexane, 1:1) then revealed a spot of R_F 0.41. Work-up of the mixture, as described above, and column chromatography (benzene→benzene–ethyl acetate, 2:1) of the product afforded **13** (89 mg, 60%), $[\alpha]_D$ −1° (*c* 2.75) {lit.[4a] $[\alpha]_D$ −38.4° (*c* 3.4) for the L form}; ν_{max}^{KBr} 3460 (OH), 1790 (γ-lactone C=O), 1375 (CMe_2), and 860 cm^{-1} (dioxolane ring). N.m.r. data (acetone-d_6): δ 4.63 (s, 1 H, H-3), 4.55 (t, 1 H, $J_{4,5}$ 3 Hz, H-4), 4.46 (t, 1 H, $J_{HO,5}$ 6 Hz, HO-5), 3.85 (dd, 2 H, 2 H-5), 1.60 (s, 3 H, Me-2), and 1.35 (s, 6 H, CMe_2).

Conventional treatment of **13** (84 mg, 0.4 mmol) with dry pyridine (2 mL) and acetic anhydride (1 mL) gave the syrupy 5-acetate, which was purified by column chromatography (ethyl acetate–hexane, 1:3) to yield material (94 mg, 92%) having $[\alpha]_D$ −0.6° (*c* 3.4). R_F 0.59 (ethyl acetate–hexane, 1:1); ν_{max}^{film} 1785 (γ-lactone C=O), 1745 (acetate C=O), 1370 (CMe_2), 1240 (acetate C-O), and 850 cm^{-1} (dioxolane ring). N.m.r. data: δ 4.75 (t, 1 H, $J_{4,5}$ 3.75 Hz, H-4), 5.53 (s, 1 H, H-3), 4.35 (d, 2 H, 2 H-5), 2.10 (s, 3 H, Ac), 1.65 (s, 3 H, Me-2), and 1.44 (s, 6 H, CMe_2). Mass spectrum: *m/z* 245 ($M^+ + 1$), 229 (M^+ – Me), 216 (M^+ – CO), 186 (M^+ – Me_2CO), 184 (M^+ – AcOH), 169 (M^+ – Me – AcOH), 145, 143, 126 (M^+ – Me_2CO – AcOH), 100, 99, 85, 83, 71, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Hydrolysis of **6**. — A solution of **6** (580 mg, 2.3 mmol) in acetic acid–water (1:1, 10 mL) was kept at 50° for 1.5 h. T.l.c. (ether–hexane, 2:1) then showed that **6** had disappeared. Evaporation of the solvent and removal of the remaining acetic acid by codistillation with water afforded a syrupy residue (489 mg) that was acetonated (15 mL, dry acetone) for 24 h in the presence of anhydrous copper sulfate (1.5 g) and toluene-*p*-sulfonic acid (100 mg). T.l.c. (ether–hexane, 2:1) of the reaction mixture revealed three spots, R_F 0.68, 0.28, and a non-mobile substance. The mixture was neutralised (anhydrous K_2CO_3), filtered, and concentrated, and the residue was subjected to column chromatography (ether–hexane, 1:2→1:1→ether–methanol, 10:1), to yield, first, syrupy ethyl 2,3:4,5-di-*O*-isopropylidene-2-*C*-methyl-DL-arabinonate (**16**, 122 mg), $[\alpha]_D$ +0.35° (*c* 1); ν_{max}^{film} 1750 (ester C=O), 1375 (CMe_2), 1050 and 840 cm^{-1} (dioxolane ring). N.m.r. data (80 MHz): δ 4.47–3.90 (m, 4 H, H-3,4,5,5'), 4.23 (q, 2 H, *J* 7 Hz, OCH_2Me), 1.45, 1.41, 1.39, 1.37, and 1.30 (5 s, 15 H, Me-2 and 2 CMe_2), and 1.28 (t, 3 H, OCH_2Me). Mass spectrum: *m/z* 273 (M^+ – Me), 259 (M^+ – C_2H_5), 215 (M^+ – Me – Me_2CO), 187 (M^+ – $C_5H_9O_2$), 169, 157 (M^+ – Me – Me_2CO – AcOH), 127 (M^+ – $C_5H_9O_2$ – AcOH), 101 ($C_5H_9O_2^+$), 99 ($C_5H_7O_2^+$), 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Eluted second was 3,4-*O*-isopropylidene-2-*C*-methyl-DL-arabinono-1,5-lactone (**17**, 40 mg), m.p. 127.5–128.5° (from ether–hexane), $[\alpha]_D$ −3° (*c* 1.1); ν_{max}^{KBr} 3460 (OH), 1735 (δ-lactone C=O), 1380 and 1375 (CMe_2), and 860 cm^{-1} (dioxolane ring). N.m.r.data (80 MHz): δ 4.91 (dd, 1 H, $J_{4,5}$ 2, $J_{5,5'}$ 13 Hz, H-5), 4.55 (dt, 1 H, $J_{3,4}$ 7.5 Hz, H-4), 4.33 (d, 1 H, H-5'), 4.30 (d, 1 H, H-3), 3.18 (s, 1 H, HO-2), 1.56 (s, 3 H, Me-2), 1.41 and 1.35 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_9H_{14}O_5$: CM 53.46; H, 6.98. Found: C, 54.03; H, 7.24.

Eluted third was 2-*C*-methyl-DL-arabinono-1,4-lactone (**18**, 260 mg), m.p. 89–91°, $[\alpha]_D$ +0.6° (*c* 1.4, methanol), R_F 0.66 (p.c.); ν_{max}^{film} 3380 (OH) and 1780 cm^{-1} (γ-lactone C=O). N.m.r. data: δ (acetone-d_6) 5.00–3.60 (m, 7 H, H-3,4,5,5', and HO-2,3,5) and 1.39 (s, 3 H, Me-2).

Anal. Calc. for $C_6H_{10}O_5$: C, 44.44; H, 6.22. Found: C, 44.46; H, 6.23.

Conventional treatment of **18** (110 mg, 0.7 mmol) with dry pyridine (2 mL) and benzoyl chloride (0.5 mL) gave the tribenzoate **19** (270 mg, 84%), m.p. 102–103°, $[\alpha]_D$ +2° (*c* 1.2), R_F 0.64 (benzene–ethyl acetate, 10:1); ν_{max}^{KBr} 1830 (γ-lactone C=O), 1735 (benzoate C=O), and 695 cm^{-1} (benzoate). N.m.r. data: δ 8.10–7.16 (2 m, 15 H, 3 Bz), 6.29 (dt, 1 H, $J_{3,4}$ 6.75, $J_{3,5}$ 2.25 Hz, H-4), 4.78 (d, 1 H, H-3), 4.75 (d, 2 H, H-5,5), and 1.79 (s, 3 H, Me-2). Mass spectrum: *m/z* 475 (M^+ + 1), 352 (M^+ − BzOH), 231 (M^+ − BzOH − BzO), 227, 189, 176, 122 ($BzOH^+$), 105 (Bz^+, base peak). and 77 (Ph^+).

Anal. Calc. for $C_{27}H_{22}O_8$: C, 68.35; H, 4.67. Found: C, 68.03; H, 4.61.

Acetonation of **18** (360 mg), using dry acetone (15 mL), conc. sulfuric acid (0.15 mL), and anhydrous copper sulfate (2 g) for 24 h, yielded **17** (50 mg) and unreacted **18** (220 mg).

Conventional treatment of **18** (186 mg, 1.15 mmol) with dry pyridine (2 mL) and acetic anhydride (1.5 mL) gave the triacetate **20** (288 mg, 87%), m.p. 88–89° (from ether), $[\alpha]_D$ 0° (*c* 2.6); ν_{max}^{KBr} 1810 (γ-lactone C=O), 1755 (acetate C=O), and 1240 cm^{-1} (acetate C-O). N.m.r. data: δ 5.72 (dt, 1 H, $J_{3,4}$ 7.5, $J_{4,5}$ 3 Hz, H-4), 4.70–4.15 (m, 3 H, H-3,5,5), 2.10 and 2.05 (2 s, 9 H, intensity ratio 1:2, 3 Ac), and 1.45 (s, 3 H, Me-2). Mass spectrum: *m/z* 289 (M^+ + 1), 246 (M^+ + 1 − Ac), 229 (M^+ + 1 − AcOH), 228 (M^+ − AcOH), 215 (M^+ − CH_2OAc), 186 (M^+ + 1 − AcOH − Ac), 168 (M^+ − AcOH − AcOH), 156, 145, 142, 127, 126, 116, 115, 103, 100, 99, 83, and 43 (Ac^+, base peak).

Anal. Calc for $C_{12}H_{16}O_8$: C, 50.00; H, 5.60. Found: C, 50.68; H, 5.07.

Reduction of **18**. — To an ice-cooled and stirred solution of **18** (2 g, 12 mmol) in water (15 mL) was added a cooled solution of sodium borohydride (1 g) in water (25 mL) at such rate that the temperature was maintained at ~3°; the pH was kept at 3–4 by the addition of 0.5M sulfuric acid. Evolution of hydrogen occurred during the addition (~1 h). After a further 20 min, 0.5M sulfuric acid (2 mL) was added to decompose the excess of hydride, and the mixture was diluted with water, stirred first with Amberlite IR-120 (H^+) resin (35 mL) and then with Lewatid MP-69 (HCO_3^-) resin (60 mL), filtered, and concentrated. Methanol was repeatedly evaporated from the residue (1 g), p.c. of which revealed **18** together with **21** (R_F

0.40). Acetonation of this mixture (0.7 g), as described below for D-**21**, gave syrupy 1,2:3,4-di-*O*-isopropylidene-2-*C*-methyl-β-DL-arabinopyranose (**22**, 250 mg), $[\alpha]_D$ 0° (*c* 1.8), which gave the same spectroscopic data as D-**22**.

Hydroxylation of ethyl trans-*2,3-dideoxy-4,5-O-isopropylidene-2-C-methyl*-D-glycero-*pent-2-enonate* (D-**2**). — Reaction of D-**2**[8] (2.14 g, 10 mmol) in ethanol–water (1:1, 50 mL) with potassium chlorate (0.65 g, 5.3 mmol) and aqueous 1% osmium tetraoxide (5 mL), as described above for **2**, gave syrupy ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-D-xylonate (D-**5**; 450 mg, 18%), $[\alpha]_D$ −15° (*c* 1.2); ν_{max}^{film} 3460 (OH), 1745 (ester C=O), 1375 (CMe_2), 1065 and 860 cm^{-1} (dioxolane ring). N.m.r. data: δ 4.28 (q, 2 H, *J* 7 Hz, OCH_2Me), 4.60–3.85 (m, 3 H, H-4,5,5′), 3.74 (s, 1 H, HO-2), 3.58 (dd, $J_{3,4}$ 3, $J_{3,HO-3}$ 10 Hz, H-3), 2.95 (d, 1 H, HO-3), 1.45, 1.41, and 1.35 (3 s, 9 H, Me-2 and CMe_2), and 1.30 (t, 3 H, OCH_2Me). Mass spectrum: *m/z* 249 ($M^+ + 1$), 233 ($M^+ - Me$), 215 ($M^+ - Me - H_2O$), 203 ($M^+ - OEt$), 191, 175 ($M^+ - CO_2Et$), 173 ($M^+ - Me - AcOH$), 159, 147 ($M^+ - C_5H_9O_2$), 145, 131, 118, 117, 101 ($C_5H_9O_2^+$), 99, 73, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

The second product isolated was ethyl 4,5-*O*-isopropylidene-2-*C*-methyl-D-arabinonate (D-**6**; 900 mg, 37%), m.p. 63–64° (from hexane), $[\alpha]_D$ +21° (*c* 1.1); ν_{max}^{film} 3465 (OH), 1740 (ester C=O), 1375 (CMe_2), 1160, 1050, and 850 cm^{-1} (dioxolane ring). N.m.r. data: δ 4.40–3.52 (m, 4 H, H-3,4,5,5′), 4.28 (q, 2 H, *J* 7 Hz, OCH_2Me), 3.71 (bs, 1 H, HO-2), 2.80 (d, 1 H, $J_{3,HO-3}$ 6.75 Hz, HO-3), 1.45 and 1.39 (2 bs, 9 H, Me-2 and CMe_2), and 1.32 (t, 3 H, OCH_2Me). Mass spectrum: *m/z* 249 ($M^+ + 1$), 233 ($M^+ - Me$), 215 ($M^+ - Me - H_2O$), 191, 175 ($M^+ - CO_2Et$), 159, 147 ($M^+ - C_5H_9O_2$), 145, 141, 131, 118, 117, 101 ($C_5H_9O_2^+$), 99, 83, 73, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_{11}H_{20}O_6$: C, 53.21; H, 8.12. Found: C, 53.29; H, 8.38.

2-C-Methyl-D-*xylono-1,4-lactone* (D-**23**). — A suspension of D-**5** (345 mg, 2.1 mmol) in M sodium hydroxide (4 mL) was heated under reflux for 30 min. T.l.c. (ether–hexane, 1:1) then revealed that D-**5** had disappeared, and the mixture was boiled under reflux with Amberlite IR-120 (H^+) resin (3 g) for 4 h, filtered, and concentrated, to give D-**23** (203 mg, 94%), m.p. 162–164° (from ethyl acetate), $[\alpha]_D$ +96.5° (*c* 3.5, water) {lit.[6] m.p. 161°, $[\alpha]_D$ +93.1° (*c* 0.8, water)}; ν_{max}^{KBr} 3400 (OH) and 1790 cm^{-1} (γ-lactone C=O). N.m.r. data: δ (Me_2SO-d_6) 6.01 (s, 1 H, HO-2), 5.57 (d, 1 H, $J_{3,HO-3}$ 5.25 Hz, HO-3), 4.82 (bt, 1 H, $J_{5,HO-5}$ 5.63 Hz, HO-5), 4.72–4.40 (m, 1 H, H-4), 3.87 (dd, 1 H, $J_{3,4}$ 3.75 Hz, H-3), 3.63 (bt, 2 H, H-5,5′), and 1.26 (s, 3 H, Me-2); δ (Me_2SO-d_6 + D_2O) 4.60 (o, 1 H, $J_{3,4}$ 3.75, $J_{4,5}$ 5.25, $J_{4,5'}$ 7.50 Hz, H-4), 3.90 (d, 1 H, $J_{3,4}$ 3.75 Hz, H-3), 3.75–3.55 (m, 2 H, H-5,5′), and 1.22 (s, 3 H, Me-2). Mass spectrum: *m/z* 163 ($M^+ + 1$), 162 (M^+), 145 ($M^+ - OH$), 144 ($M^+ - H_2O$), 117 ($M^+ - OH - CO$), 116 ($M^+ - H_2O - CO$), 103, 91, 87, 74, and 43 (Ac^+, base peak).

Anal. Calc. for $C_6H_{10}O_5$: C, 44.44; H, 6.22. Found: C, 44.45; H, 6.19.

3,5-O-Isopropylidene-2-C-methyl-D-*xylono-1,4-lactone* (D-**24**). — A mixture of D-**23** (113 mg, 0.7 mmol), acetone (5 mL), and conc. sulfuric acid (0.1 mL) was

stirred with powdered, anhydrous copper sulfate (500 mg) for 24 h. The usual work-up then gave, after column chromatography (benzene→benzene–ethyl acetate, 2:1), D-**24** (50 mg), m.p. 153–154°, $[\alpha]_D$ +69° (*c* 0.9) {lit.[7] L form, m.p. 155–157°, $[\alpha]_D$ −73° (*c* 1.95)}; ν_{max}^{KBr} 3460 (OH), 1780 γ-lactone C=O), and 1385 cm^{-1} (CMe_2). N.m.r. data: δ (acetone-d_6) 5.22 (bs, 1 H, HO-2), 4.55 (q, 1 H, $J_{3,4} = J_{4,5} = J_{4,5'} = 2.25$ Hz, H-4), 4.30 (dd, 1 H, $J_{5,5'}$ 13 Hz, H-5), 4.22 (d, 1 H, H-3), 4.01 (dd, 1 H, H-5'), 1.50, 1.35, and 1.30 (3 s, 9 H, Me-2 and CMe_2). Mass spectrum: *m/z* 203 ($M^+ + 1$), 187 ($M^+ - Me$), 159 ($M^+ - Me - CO$), 145, 144 ($M^+ - Me_2CO$), 127 ($M^+ - Me - AcOH$), 99 ($M^+ - Me - CO - AcOH$), 83, 71, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_9H_{14}O_5$: C, 53.46; H, 6.93. Found: C, 53.44; H, 7.09.

Conventional treatment of D-**24** (22 mg) with acetic anhydride–pyridine and column chromatography (ether–hexane, 2:3) of the product afforded the 2-acetate D-**25** (20 mg), m.p. 88–90°, $[\alpha]_D$ +53° (*c* 0.8), R_F 0.27 (ether–hexane, 3:2); ν_{max}^{KBr} 1780 (γ-lactone C=O), 1750 (acetate C=O), 1370 (CMe_2), and 1215 cm^{-1} (acetate C-O). N.m.r. data: δ 4.80–4.48 (m, 2 H, H-3,4), 4.29–3.68 (m, 2 H, H-5,5'), 2.14 (s, 3 H, Ac), 1.65, 1.45, and 1.41 (3 s, 9 H, Me-2 and CMe_2). Mass spectrum: *m/z* 245 ($M^+ + 1$), 229 ($M^+ - Me$), 184 ($M^+ - AcOH$), 169 ($M^+ - Me - AcOH$), 144, 127, 83, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 53.83; H, 6.55.

*2-C-Methyl-*D*-arabinono-1,4-lactone* (D-**18**). — A suspension of the D-**6** (668 mg, 4.1 mmol) in M sodium hydroxide (6 mL) was boiled under reflux for 4 h. T.l.c. (ether–hexane, 1:1) then showed that D-**6** had disappeared. Amberlite IR-120 (H^+) resin (5 g) was added, the mixture was boiled, the resin was collected and washed with water, and the combined filtrate and washings were concentrated to give, after column chromatography, syrupy D-**18** (420 mg, 81%), $[\alpha]_D$ +69° (*c* 1.6, water) {lit.[7] $[\alpha]_D$ +82.5° (*c* 0.9, water) for the monohydrate}; ν_{max}^{film} 3400 (OH) and 1790 cm^{-1} (γ-lactone C=O). N.m.r. data: δ 5.08 (m, 2 H, HO-3,5), 4.62–3.67 (m, 4 H, H-3,4,5,5'), 3.45 (s, 1 H, HO-2), and 1.38 (s, 3 H, Me-2). Mass spectrum: *m/z* 163 ($M^+ + 1$), 162 (M^+), 135, 117 ($M^+ - OH - CO$), 116 ($M^+ - H_2O - CO$), 103, 87, 74, and 43 (Ac^+, base peak).

Conventional treatment of D-**18** (50 mg, 0.3 mmol) with pyridine (1 mL) and benzoyl chloride (0.5 mL) gave the tribenzoate D-**19** (130 mg, 89%), $[\alpha]_D$ +12° (*c* 1.45). I.r. and n.m.r. data accorded with those for **19**. Mass spectrum: *m/z* 475 ($M^+ + 1$), 352 ($M^+ - BzOH$), 231 ($M^+ - BzOH - BzO$), 227, 105 (Bz^+, base peak), and 77 (Ph^+).

Conventional treatment of D-**18** (70 mg, 0.4 mmol) with pyridine (1.5 mL) and acetic anhydride (1 mL) gave the syrupy triacetate D-**20** (94 mg, 76%), $[\alpha]_D$ +64.2° (*c* 1). The i.r. and n.m.r. data accorded with those for **20**. Mass spectrum: *m/z* 289 ($M^+ + 1$), 229 ($M^+ - AcO$), 228 ($M^+ - AcOH$), 186 ($M^+ - AcO - AcOH$), 168 ($M^+ - 2\ AcOH$), 103, 100, 83, and 43 (Ac^+, base peak).

*1,2:3,4-Di-*O*-isopropylidene-2-C-methyl-β-*D*-arabinopyranose* (D-**22**). — A solution of 2-C-methyl-D-arabinose[4f] (D-**21**; 70 mg, 0.42 mmol) in dry acetone (10

mL) and conc. sulfuric acid (0.1 mL) was stirred with powdered, anhydrous copper sulfate (2 g) at room temperature overnight. T.l.c. (ethyl acetate–light petroleum, 1:4) then revealed a spot of R_F 0.64. The mixture was neutralised (anhydrous K_2CO_3), filtered, and concentrated. Column chromatography (ethyl acetate–light petroleum, 1:4) of the residue gave D-**22** (93 mg, 89%), m.p. 66–68°, $[\alpha]_D$ +12° (*c* 1.4); ν_{max}^{film} 1375 cm^{-1} (CMe_2). N.m.r. data: δ 5.26 (s, 1 H, H-1), 4.30 (d, 1 H, $J_{3,4}$ 1.5 Hz, H-3), 4.29 (m, 1 H, H-4), 3.94 (dd, 1 H, $J_{4,5}$ 2.1 Hz, H-5), 3.56 (dd, 1 H, $J_{4,5'}$ 2.25, $J_{5,5'}$ 13 Hz, H-5'), 1.50, 1.46, and 1.34 (3 s, 15 H, intensity ratios 3:1:1, Me-2 and 2 CMe_2). Mass spectrum: *m/z* 245 (M^+ + 1), 244 (M^+), 229 (M^+ – Me), 187, 171 (M^+ – Me – Me_2CO), 169 (M^+ – Me –AcOH), 157, 143, 129, 114 ($C_6H_{10}O_2^+$), 111 (M^+ – Me – Me_2CO – AcOH), 101, 100 ($C_5H_8O_2^+$), 99, ($C_6H_{10}O_2^+$ – Me), 85 ($C_5H_8O_2^+$ – Me), 83 ($C_5H_7O_2^+$), 69 ($C_4H_5O^+$), 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92. Found: C, 60.25; H, 6.04.

Reduction of D-**18**. — A solution of D-**18** (250 mg, 1.5 mmol) in water (2 mL) was treated at 0° with M sodium borohydride (2 mL). The mixture was stored at room temperature overnight, diluted with water (15 mL), treated with Amberlite IR-120 (H^+) resin (10 g), and, after 3 h, filtered, and concentrated; methanol was then repeatedly evaporated from the residue to remove boric acid. T.l.c. (ether–methanol, 9:1) then revealed D-**18** and a new compound R_F 0.16. Acetonation of this mixture, as described before, gave D-**22** (17 mg), m.p. 66–67°, $[\alpha]_D$ +10.5° (*c* 1.55). The i.r. and n.m.r. data accorded with those already described.

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